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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,705	03/08/2006	Gaetano T. Montelione	RUT0001-00US	9294

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EXAMINER

STEELE, AMBER D

ART UNIT	PAPER NUMBER
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1639

MAIL DATE	DELIVERY MODE
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03/09/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/536,705	Applicant(s) MONTELIONE ET AL.	
	Examiner AMBER D. STEELE	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 94-113 is/are pending in the application.
- 4a) Of the above claim(s) 94-97, 101, 104, 105, 109 and 111-113 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 98-100, 102-103, 106-108, and 110 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 May 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9/30/05</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply</u> . |

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DETAILED ACTION

Status of the Claims

1. Claims 1-93 were originally filed on May 27, 2005.

The preliminary amendment received on June 4, 2008 canceled claims 1-93 and added new claims 94-113.

The amendment received on January 23, 2009 amended claims 100, 103, 107, and 111.

Election/Restrictions

2. Applicant's election with traverse of Group II (claims 98-110) in the reply filed on January 23, 2009 is acknowledged. The traversal is on the ground(s) that a search burden does not exist. This is not found persuasive because the present application is a National Stage (371) application. Therefore, the restriction is based on Lack of Unity (see MPEP § 823 and § 1893.03(d)). Since arguments regarding the Lack of Unity were not presented, the arguments are not persuasive.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 94-97 and 111-113 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on January 23, 2009.

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4. Applicant's election without traverse of simultaneous addition as the species of when the candidate compound is added and fluorescent label as the species of label in the reply filed on January 23, 2009 is acknowledged.

5. Claims 101, 104-105, and 109 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 23, 2009.

6. Applicant's election with traverse of fluorescence polarization anisotropy as the species of detection in the reply filed on January 23, 2009 is acknowledged. The traversal is on the ground(s) that fluorescence polarization anisotropy can be performed in a high-throughput manner. This is found persuasive. Therefore, the claims to high-throughput screening via array have not been withdrawn from consideration.

Priority

7. The present application claims status as a National Stage (371) of PCT/US04/20244 filed June 26, 2004 which claims benefit of provisional application 60/482,722 filed June 27, 2003.

Information Disclosure Statement

8. The information disclosure statement (IDS) submitted on September 30, 2005 is being considered by the examiner.

Sequence Compliance

9. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However,

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this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. See Figure 1A.

Drawings

10. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Figure 2C.

Corrected drawing sheets in compliance with 37 CFR 1.121(d), **or amendment to the specification to add the reference character(s) in the description** in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

11. The abstract of the disclosure is objected to because of the following: in the first sentence, “specie” should be “species” and the sentence should be properly punctuated; in the second sentence, “to tested” should be “to be tested” and “detecting presence” should be “detecting the presence”; and in the third sentence, “control bacterial growth” should be “control of bacterial growth”. Correction is required. See MPEP § 608.01(b).

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12. The disclosure is objected to because of the following informalities: the first line of the specification should be amended to include PCT/US04/20244.

Appropriate correction is required.

13. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See page 33, lines 19-20.

14. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

15. Claims 98-100, 102-103, 106-108, and 110 are objected to because of the following informalities: claim 98, method step b reads “detecting extent”. “[D]etecting the extent” is suggested. Appropriate correction is required.

Invention as Claimed

16. A method of identifying compounds having inhibitory activity against a bacterial strain comprising (a) preparing a reaction system comprising a bacterial RlmA protein or a rRNA binding domain thereof, a rRNA that binds said protein or binding domain thereof, and a candidate compound, (b) detecting extent of binding between the bacterial RlmA protein and the rRNA wherein reduced binding between the bacterial RlmA protein and the rRNA in the

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presence of the compound relative to a control is indicative of inhibitory activity of the compound against the bacterial strain, and variations thereof.

Claim Rejections - 35 USC § 112

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 98-100, 102-103, 106-108, and 110 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Independent claim 98 is drawn to a method of identifying compounds having inhibitory activity against a bacterial strain comprising (a) preparing a reaction system comprising a bacterial RlmA protein or a rRNA binding domain thereof, a rRNA that binds said protein or binding domain thereof, and a candidate compound and (b) detecting extent of binding between the bacterial RlmA protein and the rRNA wherein reduced binding between the bacterial RlmA protein and the rRNA in the presence of the compound relative to a control is indicative of inhibitory activity of the compound against the bacterial strain. The invention as claimed encompasses all known candidate compounds and all potential candidate compounds since

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virtually any candidate compound can be screened for inhibition. In addition, the invention as claimed encompasses all known rRNA binding domains and all potential rRNA binding domains since virtually any rRNA binding domain can bind under various conditions (e.g. nonspecific binding, etc.). The claimed invention does not include any structural information regarding the rRNA binding domain (i.e. the rRNA binding domain presumably binds rRNA which is functional language). In addition, the claimed invention does not include any structural information regarding the candidate compound (i.e. inhibitory activity is functional language).

The specification teaches RImAI and RImAII (see examples). However, the specification does not teach a single species of candidate compound (i.e. final product of the method of independent claim 98). Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed since applicants have not disclosed a single candidate compound.

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of RImAI and RImAII as disclosed by the specification, the skilled artisan cannot envision the method of independent claim 98. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen

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Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d

1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 98-100, 102-103, 106-108, and 110 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 98 recites the limitation "said protein" in line 2 of method step a. There is insufficient antecedent basis for this limitation in the claim.

B. Claim 98 recites the limitation "said...binding domain" in line 2 of method step a. There is insufficient antecedent basis for this limitation in the claim.

C. Claim 98 recites the limitation "the compound" in line 3 of method step b. There is insufficient antecedent basis for this limitation in the claim.

D. Claim 102 recites the limitation "the detectable label" in line 2. There is insufficient antecedent basis for this limitation in the claim.

21. Claims 98-100, 102-103, 106-108, and 110 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. Method step (a) of independent claim 98 requires "preparing a reaction system comprising a bacterial RlmA protein or a rRNA binding

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domain thereof, a rRNA, and a candidate compound” while method step (b) requires “detecting [the] extent of binding between the bacterial RlmA protein and the rRNA”. Therefore, it is not clear if method step (b) is optional or not. For example, if the reaction system comprises a rRNA binding domain, a rRNA, and a candidate compound, it is not clear how one could detect binding between bacterial RlmA and rRNA since RlmA is not part of the reaction system.

Claim Rejections - 35 USC § 102

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

23. Claim 98 is rejected under 35 U.S.C. 102(b) as being anticipated by Gustafsson et al., 1998, Identification of the rrmA Gene Encoding the 23S rRNA m¹G745 Methyltransferase in *Escherichia coli* and Characterization of an m¹G745-Deficient Mutant, Journal of Bacteriology, 180(2): 359-365 (provided by applicants in the IDS).

For present claim 98, Gustafsson et al. teach methods of identifying compounds that inhibit bacterial growth comprising (a) providing a cell comprising RlmA (i.e. RlmAI or rrmA) and rRNA, (b) providing a candidate compound, and (c) detecting inhibitory activity of the compound against the bacterial strain compared to control (i.e. disruption of binding, decreased growth; please refer to the entire reference particularly the abstract; pages 362-363).

Therefore, the teachings of Gustafsson et al. anticipate the presently claimed invention.

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24. Claims 98-100, 102-103, 106-108, and 110 are rejected under 35 U.S.C. 102(e) as being anticipated by Yuan U.S. Patent 6,610,504.

For present claim 98, Yuan teaches methods of screening for inhibitors comprising (a) preparing a reaction system comprising a rRNA binding domain, a rRNA, and a candidate compound and (b) detecting if the candidate compound inhibits activity of the reaction system via altering binding between the rRNA binding domain and the rRNA via utilizing a control (please refer to the entire specification particularly the abstract; columns 2-4, 7, 9-10, 12, 13-17, 29-30, 32-38, 57-59; Table 2).

For present claims 99 and 110, Yuan teaches high throughput assays and solid supports (please refer to the entire specification particularly columns 4, 7, 15, 30, 32-33, 36-37, 44).

For present claim 100, Yuan teaches reaction mixtures wherein all reagents are added simultaneously (please refer to the entire specification particularly column 30).

For present claims 102-103 and 106, Yuan teaches fluorescent labels (please refer to the entire specification particularly columns 34-36, 79).

For present claims 107-108, Yuan teaches fluorescence polarization anisotropy (please refer to the entire specification particularly columns 4, 36).

Therefore, the presently claimed invention is anticipated by the teachings of Yuan.

Claim Rejections - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

26. Claims 98-100, 102-103, 106-108, and 110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yuan U.S. Patent 6,610,504 and Liu et al., 2002, Resistance to the macrolide antibiotic tylosin is conferred by single methylations at 23S rRNA nucleotides G748 and A2058 acting in synergy, PNAS, 99(23): 14658-14663 (provided by applicants in the IDS).

For present claim 98, Yuan teaches methods of screening for methyltransferase (i.e. SAM methyltransferases preferred) inhibitors comprising (a) preparing a reaction system comprising a rRNA binding domain including rRNA methyltransferases, a rRNA, and a candidate compound and (b) detecting if the candidate compound inhibits activity of the reaction system via altering binding between the rRNA binding domain and the rRNA via utilizing a control (please refer to the entire specification particularly the abstract; columns 2-4, 7, 9-10, 12, 13-17, 29-30, 32-38, 57-59; Table 2).

For present claims 99 and 110, Yuan teaches high throughput assays and solid supports (please refer to the entire specification particularly columns 4, 7, 15, 30, 32-33, 36-37, 44).

For present claim 100, Yuan teaches reaction mixtures wherein all reagents are added simultaneously (please refer to the entire specification particularly column 30).

For present claims 102-103 and 106, Yuan teaches fluorescent labels (please refer to the entire specification particularly columns 34-36, 79).

For present claims 107-108, Yuan teaches fluorescence polarization anisotropy (please refer to the entire specification particularly columns 4, 36).

However, Yuan does not specifically teach the rRNA methyltransferase RlmA.

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For present claim 98, Liu et al. teach methods of screening comprising (a) providing a reaction system comprising RlmAI (i.e. rrmA) or RlmAII (i.e. tlrB or myrA), rRNA, and a candidate compound and (b) determining if the candidate compound alters bacterial growth compared to control (please refer to the entire reference particularly the abstract; pages 14659-14660; Tables 1-3).

The claims would have been obvious because the substitution of one known element (i.e. rRNA methyltransferase genus or specific species of trmA, trmD, etc. taught by Yuan in Table 2) for another (i.e. RlmA taught by Liu et al.) would have yielded predictable results to one of ordinary skill in the art at the time of the invention (i.e. inhibition of RlmA specific activity, discovery of antibiotics that are not resistant in the presence of RlmA). See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Patent Examiner, Art Unit 1639

March 3, 2009